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PRIVY COUNCIL

31 May 1956

Dear Dr Lederberg,

Thank you for your letter of May 27. I am sending off separately some ampoules of penicillinase which would probably last you for a very long time, and would save you the necessity of growing up a culture and preparing some yourself. If you also want subcultures of strains 5 and 5B, I would be very pleased to send you these as well. Perhaps you could let me know about this.

We are doing a little work at the moment ourselves on fixation of radiopenicillin by the different strains including, of course, strain 5 and we would not like to overlap with any work Professor Johnson is doing along these lines. I think, however, this is rather unlikely as we are not concerned with the action of penicillin as an antibiotic. If, therefore, Johnson would like to work with strain 5, I should be only too delighted to send him a sample. I will wait to hear from him or you on this matter.

The "normal function" of penicillinase is, of course, a matter we are worried a lot about. From an evolutionary point of view, I do not think it is surprising to find the development of this enzyme in strains of B.cereus, which is a soil and water organism and, therefore, may well have encountered penicillins of various kinds in the soil during its evolutionary history. This seems especially more likely now that the range of different types of penicillins is known to be wider than was at first expected. I think the occurrence of penicillin, or at least, substances closely related to penicillin may be much commoner than most people realise.

We have done a bit of work on substrate and inducer specificity for penicillinase, and although I gave a paper at Brussels last year, the work has not yet been written up. I will send you a copy as soon as it has. The side chain does not appear to affect the function of penicillin either as a substrate or an inducer very greatly, but - with one exception - any "tampering" with the penicillin nucleus completely destroys its property to function either as substrate or inducer. The exception is a most interesting substance - Cephalosporin C - produced by a species of Cephalosporium and discovered by Abraham and Newton. It is chemically very closely related to amino-adipic penicillin (= cephalosporin N) and does not yield penicillamine as a breakdown product. This Cephalosporin C is the most powerful inducer of penicillinase in B.cereus we have yet encountered, but is not apparently attacked by the enzyme at all. It appears to compete with benzylpenicillin to react with the "induction centre" and I suspect that

it competes with benzylpenicillin also for combination with the specific penicillin receptor in the cell.

I hear you may be visiting Australia next year and I hope there may be a chance that you will visit this country on your way there or on your way back. It would be a great pleasure to have the chance of meeting you and I very much hope such an opportunity will arise.

Yours sincerely,

Martin Pollock

M. R. Pollock.

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